Breath Therapeutics, a Zambon company, initiates BOSTON-3 and BOSTON-4, two additional clinical studies for the treatment of bronchiolitis obliterans syndrome (BOS)

- Liposomal Cyclosporine A for Inhalation (LCsAi) is advancing in clinical studies for the treatment for bronchiolitis obliterans syndrome (BOS)
- BOS is a devastating rare lung disease associated with high mortality
- An estimated 30,000 lung transplant and allogeneic hematopoietic stem cell transplant (alloHSCT) recipients worldwide are affected by BOS[1]
- BOSTON-1 and BOSTON-2 are pivotal Phase 3 studies currently underway
- BOSTON-3 is an open-label extension study of the pivotal trials in which eligible participants will receive L-CsA-i
- BOSTON-4 is a safety and tolerability study of LCsAi in adults with BOS following alloHSCT

Milan, Italy, Munich, Germany and Menlo Park, Calif. – February 20, 2020 – Zambon, a multinational pharmaceutical company that focuses on innovation and development with the aim to improve the quality of people's health and patients' lives**,** and **Breath Therapeutics, a Zambon company**, specializing in advanced inhaled therapeutics for severe respiratory diseases, announced today the initiation of the BOSTON-4 phase 2 multi-center clinical study of Liposomal Cyclosporine A for Inhalation (LCsAi) for the treatment of bronchiolitis obliterans syndrome (BOS) following allogeneic hematopoietic stem cell transplant (alloHSCT). Additionally, the BOSTON-3 open-label extension study has been initiated and is open to eligible participants who complete the BOSTON1 and 2 phase 3 studies currently underway to evaluate LCsAi for the treatment of BOS following lung transplantation.

Anne Bergeron, MD, PhD, Prof, Hôpital Saint Louis, Paris said, "Bronchiolitis obliterans syndrome is the primary noninfectious pulmonary complication in patients who undergo allogeneic HSCT. Despite increased overall survival of alloHSCT patients over the last 20 years, there has been no significant therapeutic progress in the management of bronchiolitis obliterans syndrome, which remains a major prognostic factor in allogeneic HSCT. New directed therapies are urgently needed in the treatment of BOS. With successful development and regulatory approvals, LCsAi has the potential to become the first therapy for patients who develop this debilitating and fatal condition."

Noreen R. Henig, MD, Chief Medical Officer at Breath Therapeutics, a Zambon company, stated, "We are pleased with the significant advancements we've achieved in the development of LCsAi for the treatment of BOS. The robust BOSTON development plan will provide essential information about the safety and efficacy of L-CsA-i for most patients suffering from BOS. With BOSTON1, -2, -3, and -4, we focus on two populations with a high incidence and prevalence of

BOS – patients with BOS following lung transplant or BOS following alloHSCT. Our BOSTON1 and 2 pivotal studies are well underway and, with the initiation of BOSTON-3 and -4, we are one step closer in realizing our vision of bringing LCsAi to patients with BOS."

BOSTON-4, a prospective, single-blind randomized study will assess the safety, tolerability, pharmacokinetics (PK), and exploratory efficacy and quality of life of LCsAi for the treatment of BOS in adult alloHSCT recipients. Twenty-four patients are expected to be enrolled at up to 20 centers in Germany, France, and Spain. Patients will be randomly allocated to receive either LCsAi plus standard-of-care (SOC), or liposomal placebo plus SOC for up to 12 weeks. LCsAi and placebo will be administered via the Investigational eFlow® Technology nebulizer system (PARI). Additional information is available at www.clinicaltrials.gov. (NCT04107675)

BOSTON-3, an open-label extension study, offers eligible participants who complete the BOSTON1 or BOSTON2 phase 3 studies the opportunity to receive treatment of LCsAi plus SOC regardless of the randomization arm in the prior studies. The primary endpoint is change in forced expiratory volume (FEV_1) (mL) from baseline to week 24. The study is being conducted at the same leading lung transplant centers in eight countries as the pivotal studies.

BOSTON1 and 2 phase 3 studies were initiated in March 2019 to evaluate the efficacy and safety of LCsAi in adults with BOS following a single lung (BOSTON1) or double lung (BOSTON2) transplantation. The primary endpoint is change in FEV_1 (mL) from baseline to week 48 and key secondary endpoints will include mean change in FEV_1/FVC (forced vital capacity) and time to progression of BOS. For additional information about the BOSTON1, 2 and 3 studies, visit clinicaltrials.gov (B1 NCT03657342) (B2 NCT03656926) (B3 NCT04039347)

LCsAi has received orphan drug designation for the treatment of BOS from the US Food and Drug Administration and European Medicines Agency.

Bronchiolitis Obliterans Syndrome (BOS)

Bronchiolitis Obliterans Syndrome (BOS), also known as obliterative bronchiolitis (OB), is caused by Tcell mediated inflammation that leads to blockage of bronchioles, the small and medium airways in the lungs, resulting in respiratory failure and death. BOS most commonly affects people who have received lung or allogeneic hematopoietic stem cell transplant, although it is also associated with autoimmune disease and exposure to environmental contaminants. Based on 2019 company market research, an estimated 30,000 lung transplant and alloHSCT recipients worldwide are affected by BOS.[1]

Liposomal Cyclosporine A for Inhalation (L-CsA-i)

Liposomal Cyclosporine A for Inhalation (LCsAi) is a novel liposomal formulation of cyclosporine A developed for inhaled delivery to the lungs. Calcineurin inhibitors (CNIs), like cyclosporine A, are highly potent immunosuppressive drugs and a cornerstone of lung transplant medicine. LCsAi is administered via a drug-specific Investigational eFlow® Technology nebulizer system (PARI Pharma GmbH). The investigational drug-device combination is designed to deliver LCsAi to the site of disease in the lung.

BOSTON Clinical Development Program

LCsAi is being evaluated for the treatment of BOS in patients age six and older. Five clinical trials are currently ongoing or planned. BOSTON-1 and BOSTON-2 are pivotal Phase 3 studies of adults with BOS following lung transplantation. BOSTON3 is an open-label extension study for eligible study participants who complete BOSTON1 or BOSTON2. BOSTON-4 is a safety and exploratory efficacy study and will be the first trial of LCsAi in adults with BOS following allogeneic hematopoietic stem cell transplant. BOSTON5 is a safety study in pediatric patients with BOS.

About Zambon S.p.A.

Zambon is a multinational pharmaceutical company that focuses on innovation and development with the aim to improve patients' lives. Based on a valuable heritage and strongly focused on the future, its goal is to improve people's health through the development of innovative and quality healthcare solutions.
Zambon products are commercialized in 87 countries. The company has 20 subsidiaries in three different continents – Europe, America and Asia – and owns manufacturing units in Italy, Switzerland, China and Brazil. The company today has a strong focus on the treatment of rare diseases and specialties, on top of respiratory, pain management and women's care. Zambon was established in 1906 in Italy and today counts 2,500 employees all over the world. For further information, please visit www.zambon.com

About Breath Therapeutics, a Zambon company

Founded in 2016, Breath Therapeutics is a biopharmaceutical company specializing in advanced inhaled therapeutics for severe respiratory diseases with high unmet medical need. The company's proprietary drug formulation has been specifically designed for inhaled administration with exclusively licensed, high performance nebulizer technology. LCsAi is advancing in clinical trials for the treatment of BOS, a rare and devastating lung disease with no currently approved treatments. In July 2019, Breath Therapeutics was acquired by Zambon S.p.A, a multinational pharmaceutical company that focuses on innovation and development with the aim to improve patients' lives. Breath Therapeutics has offices in Munich, Germany and Menlo Park, California. For more information, please visit www.breath-therapeutics.com.

LCsAi and the eFlow® for L-CsA-i are investigational and their safety and efficacy have not been established for the uses described here.

Reference:
1. Data on File, Breath Therapeutics, a Zambon company, 2019.

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